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CASE REPORT

A patient with relapsing pneumonia

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Summary
Bronchiolitis obliterans organizing pneumonia (BOOP) is an inflammatory lung disease characterised by polypoid masses of granulation tissue within bronchioles, alveolar ducts and alveoli. Most commonly BOOP is idiopathic, but it can be induced by a variety of conditions. We report a case of BOOP in a 37-year-old patient with relapsing pneumonia. The patient has two daughters with cystic fibrosis and although confirmatory testing was negative, we belief that the patient has a mild variant of cystic fibrosis. To our knowledge there is only one other case report describing BOOP in a patient with cystic fibrosis.

Introduction

Bronchiolitis obliterans organizing pneumonia (BOOP) is an inflammatory lung disease and the diagnosis can be challenging owing to the non-specific symptoms. We present a case of BOOP in a 37-year-old patient with relapsing pneumonia. Our patient is remarkable because of the suspicion of a mild variant of cystic fibrosis.

Case report

A 37-year-old man was referred to our hospital because of pneumonia of the right upper lobe that did not respond to treatment with IV meropenem. Despite a switch in antimicrobial treatment to piperacilline–tazobactam and subsequently to cefepime there was no clinical or biochemical improvement. Sputum cultures and bronchial aspirates could not identify a responsible bacteria.

The patient's medical history was remarkable for ''chronic bronchitis'' during childhood and a progressive chronic renal failure due to nephroangiosclerosis requiring hemodialysis since the age of 36. In the past three years he developed five consecutive pneumonias in both lungs. Sputum cultures taken during these different episodes identified the following pathogens: *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Moraxella catarrhalis* and *Aspergillus fumigatus*. Although treatment with culture guided broad-spectrum antibiotics proved successful each time, the patient relapsed after a few months. Four months before admission treatment with voriconazole was started because of growth of *A. fumigatus* in a bronchial aspirate

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and signs of invasive aspergillosis of the right middle lobe on a computed tomography (CT) scan of the thorax.

Family history revealed two daughters with cystic fibrosis and although a F508 mutation of the CFTR gene was demonstrated in the patient, a sweat test was repeatedly negative. The patient had smoked one pack of cigarettes a day for 20 years, but smoking cessation was achieved two years ago. There were no known allergies and no exposure to toxic substances.

On admission, his temperature was 38.5 °C, blood pressure 120/66 mmHg, pulse rate 110/min and regular, respiratory frequency 20 breaths per minute and the oxygen saturation 98%. Lung auscultation revealed bilateral ronchi, cardiac and abdominal examination were normal and no lymphadenopathy was found. Laboratory studies revealed a C-reactive protein of 133 mg/L, a white blood count of 15,000/L with 79% neutrophils, chronic renal failure (urea 43 mg/dL, creatinine 3.0 mg/dL) and cholestatic liver function tests (aspartate transaminase 45 U/L, alanine transaminase 25 U/L, alkaline phosphatase 1568 U/L, Gamma glutamyl transpeptidase 987 U/L, lactate dehydrogenase 287 U/L). Chest radiography (Fig. 1) demonstrated a consolidation in the base of the right upper lobe. Both lungs showed extensive signs of chronic bronchial disease (bronchial wall thickening, bronchiectasis, peribronchial infiltration) and signs of lung destruction. A CT scan of the thorax (Fig. 2) showed consolidation with an air bronchogram in the lateral segment of the right upper lobe and surrounding ground glass opacities. On the fifth hospital day a transthoracic puncture biopsy was performed of the consolidation in the right upper lobe. Microscopy (Fig. 3) demonstrated granulation tissue and fibroblastic proliferation within bronchioles, alveolar ducts and alveoli, associated with a mononuclear interstitial infiltrate. There were no signs of infection or fungi. The diagnosis of *Bronchiolitis obliterans* organizing pneumonia (BOOP) was made. Antibiotics were stopped and treatment with intravenous methylprednisolone 40 mg once daily was started with rapid clinical and biochemical improvement within 48 h. At 1 month of follow-up there is no relapse and the dose of methylprednisolone is slowly being tapered. The patient is a candidate for a combined renal-lung transplantation. Although confirmatory testing was negative, there remains a high suspicion of underlying cystic fibrosis.

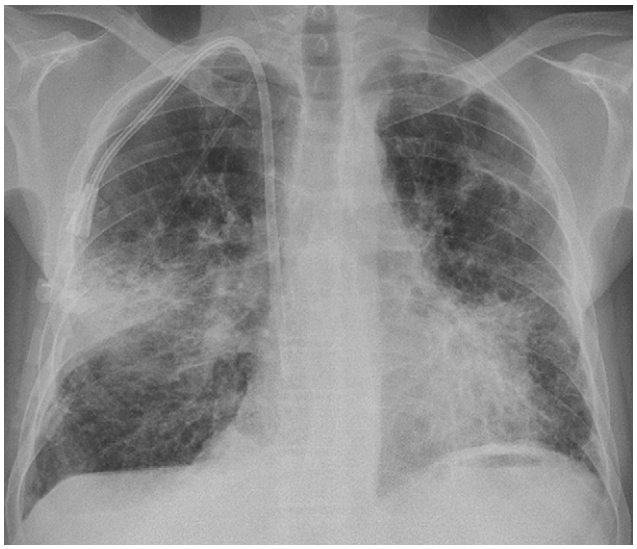

Figure 1 A supine posteroanterior chest radiography demonstrates a consolidation in the base of the right upper lobe. Both lungs show signs of chronic bronchial disease and lung destruction. At the left lung apex there is pleural thickening. A Hickmann catheter is present in the right subclavian vein.

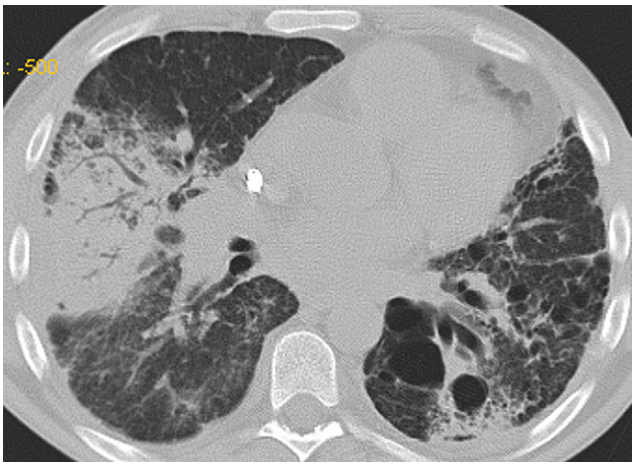

Figure 2 Spiral computed tomography scan of the chest shows consolidation with an air bronchogram in the lateral segment of the right upper lobe and surrounding ground glass opacities. There is an important destruction of the left lung parenchyma with cavities and bronchiectasis.

Discussion

Bronchiolitis obliterans organizing pneumonia is an inflammatory lung disease characterised by polypoid masses of granulation tissue within bronchioles, alveolar ducts and alveoli.[1]

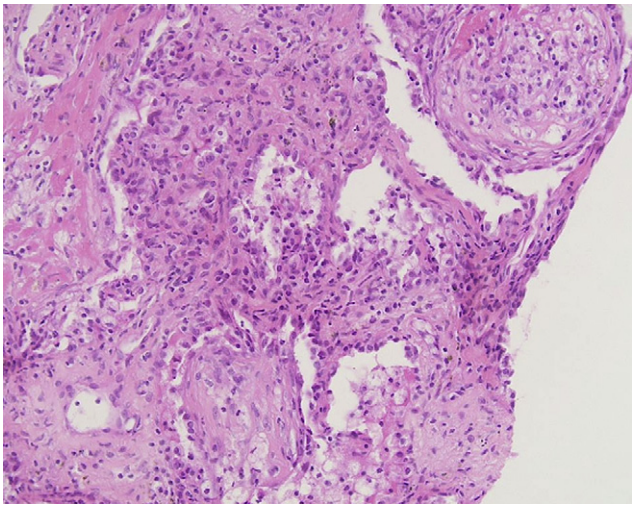

Figure 3 Transthoracic puncture biopsy stained with hematoxylin—eosin demonstrates granulation tissue and fibroblastic proliferation within bronchioles, alveolar ducts and alveoli, associated with a mononuclear interstitial infiltrate.

Most commonly BOOP is idiopathic, but it can be induced by a variety of conditions. BOOP can develop after an infectious pneumonia with bacteria (*Chlamydia*, *Legionella*, *Mycoplasma pneumoniae*, *P. aeruginosa*), viruses (parainfluenza virus, adenovirus) and fungi (*Cryptococcus neoformans*, *Pneumocystis jiroveci*).[2,3] Drug-related BOOP has been associated with the use of immunosuppressive agents including bleomycin, gold, methotrexate and antibiotics such as sulfasalazine, cephalosporins, amphotericin B and a few other drugs like amiodarone, phenytoin, carbamazepine, ticlopidine and cocaine.[2] BOOP can be secondary to virtually every rheumatologic or connective tissue disease. It has also been described after bone marrow, lung and renal transplantation.[2] Radiotherapy to the breast is also believed to prime the development of BOOP.[4] Finally there are reports of BOOP in association with a wide diversity of diseases like lymphoma, inflammatory bowel disease, alcoholic cirrhosis, cystic fibrosis and others.[2,5]

Classically BOOP presents as a flu-like illness with fever, cough and dyspnea. Lung auscultation usually reveals crackles and blood results generally show inflammation. Pulmonary function is characterised by a mild to moderate decrease in vital capacity and diffusion capacity.[2]

In rare cases the disease can progress rapidly resulting in respiratory failure within a few days.[6]

The chest radiograph typically shows bilateral patchy infiltrates that can be migratory, but there are case reports of unilateral disease as well.[7,8] Computed tomography of the chest demonstrates bilateral areas of consolidation and ground glass opacities, usually located peripherally. Sometimes nodular lesions can be present, resembling bronchial carcinoma or pulmonary metastases.[9,10]

The diagnosis of BOOP can be challenging owing to the non-specific symptoms and therefore lung biopsy is the preferred method of diagnosis. The standard treatment is prednisone 60 mg a day for 1—3 months, followed by 40 mg a day for 3 months and finally 10—20 mg a day for a total of 1 year.[2] Total recovery is seen in most patients, but one third might relapse, in which case treatment with corticosteroids is restarted.[1] In case of refractory disease to prednisone, one must consider an underlying fibrotic lung disease such as usual interstitial pneumonia (UIP) and idiopathic pulmonary fibrosis (IPF).

We suspect that in our patient the BOOP was secondary to a pneumonia with *P. aeruginosa*. Additionally, we belief that the patient has a mild variant of cystic fibrosis as he was found to be heterozygote for the most common CFTR gene mutation (F508), although a sweat test was repeatedly negative. To our knowledge there is only one other case report describing BOOP in a patient with cystic fibrosis.[5]

Conflict of interest statement

All the authors declare the absence of any potential conflict of interest.

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